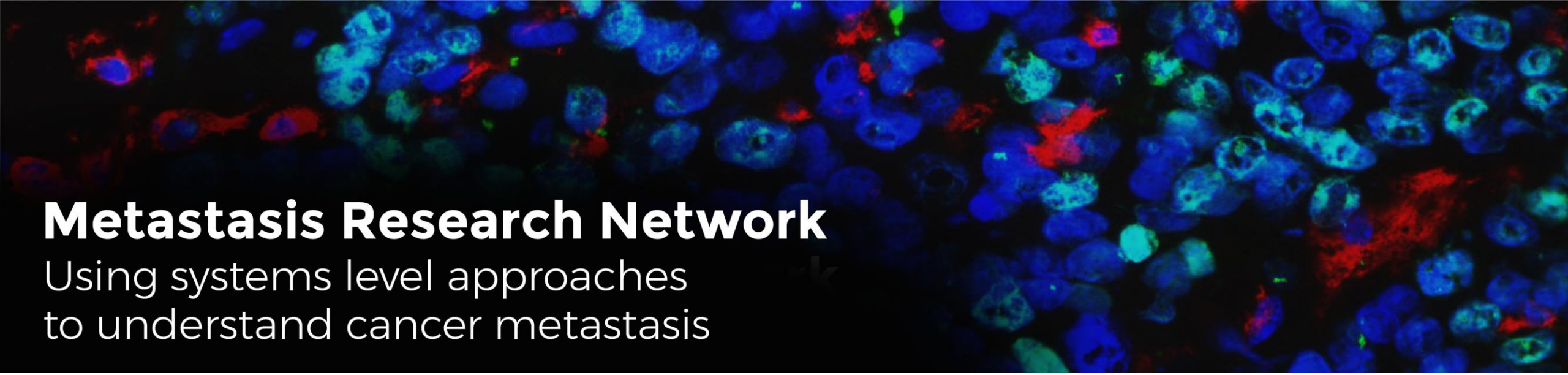

MetNet: Metastasis Research Projects (U01)
BSA Concept Presentation

June 15, 2022

MetNet Programmatic Team
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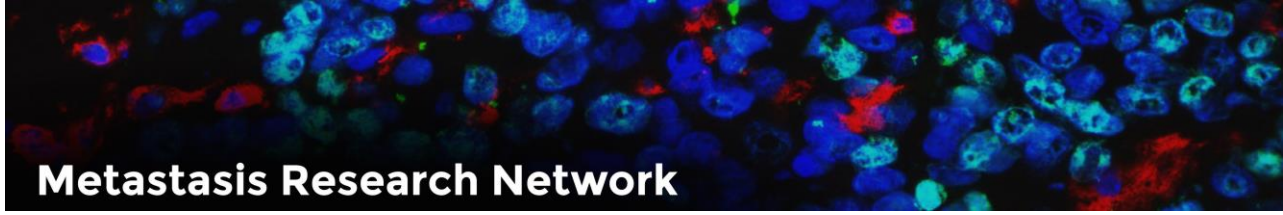
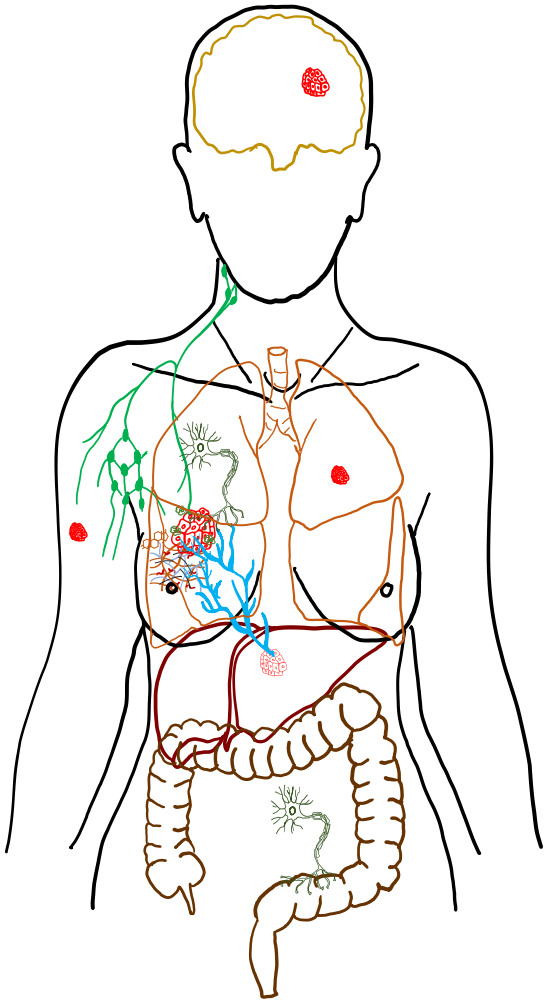
NIH NATIONAL CANCER INSTITUTE

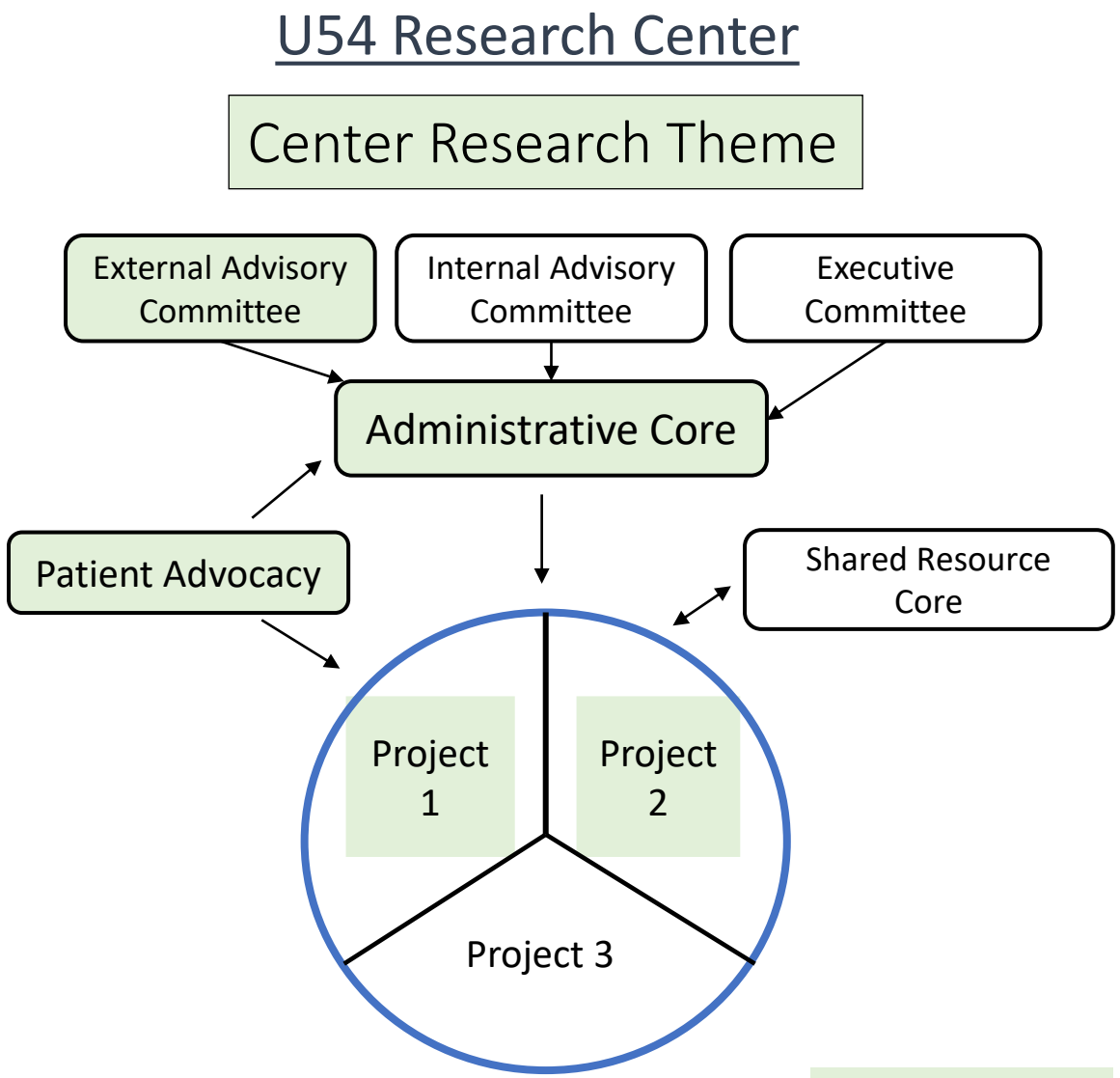
Goal of the MetNet



- Incentivize collaborative, multidisciplinary basic research to expands our mechanistic understanding of metastasis
- Use systems level approaches to account for the dynamic, non-linear, multi-scale physiological interactions – emergent processes – required for tumor cell dissemination, colonization, growth, and treatment resistance



MetNet Research Centers (U54)



Required element

Research Theme:

- Early dissemination
- Interactions/crosstalk
- Dormancy
- Responses to therapies

Working Groups

- Steering committee
- Resource and Data Sharing
- Patient Advocacy

Summary of Applications:

- 39 U54 applications received
- 4 funded

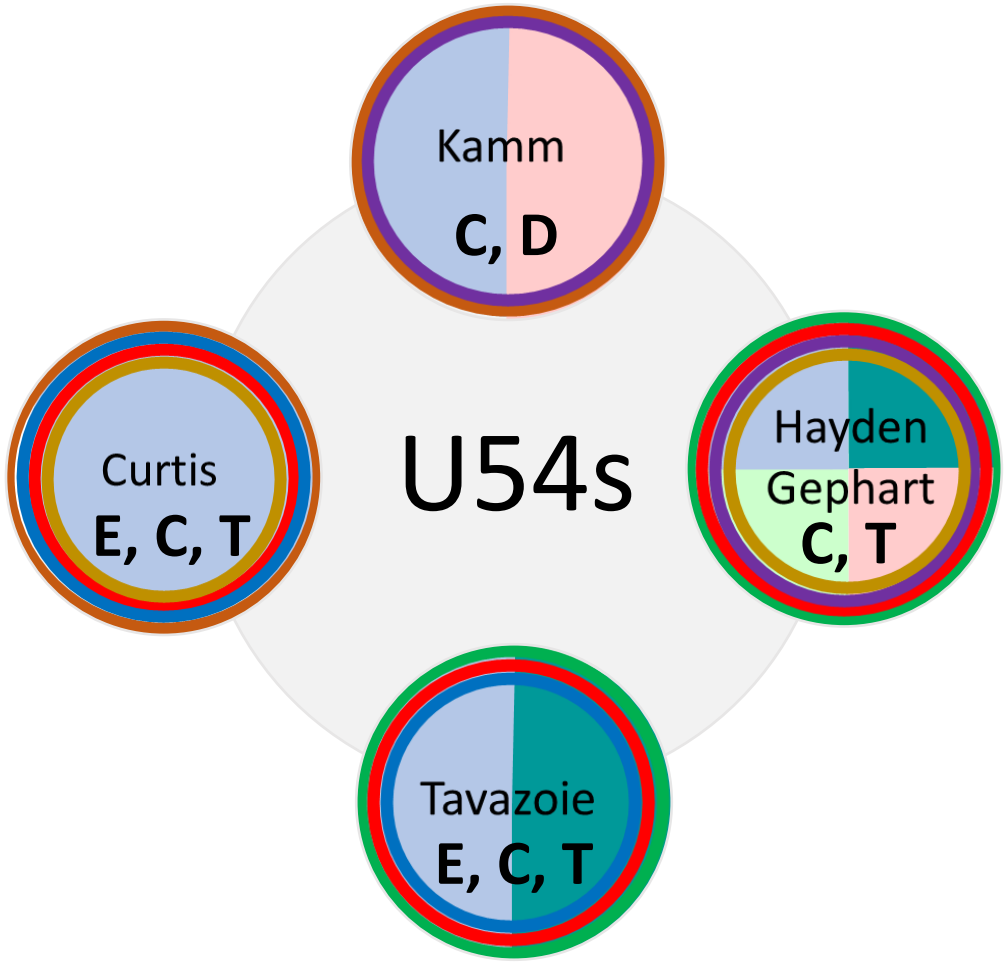
The MetNet: Integrated by shared biology, systems, and themes

Shared organ/tissue biology

- Breast to brain, liver, lung, skin
- Colon to brain, liver
- Lung to brain
- Melanoma to brain, liver, skin

Shared process or system

- ECM
- Neural Systems
- Immune System
- Drug Resistance
- Risk signature
- Vascular/Epithelial Barrier



Research Theme:

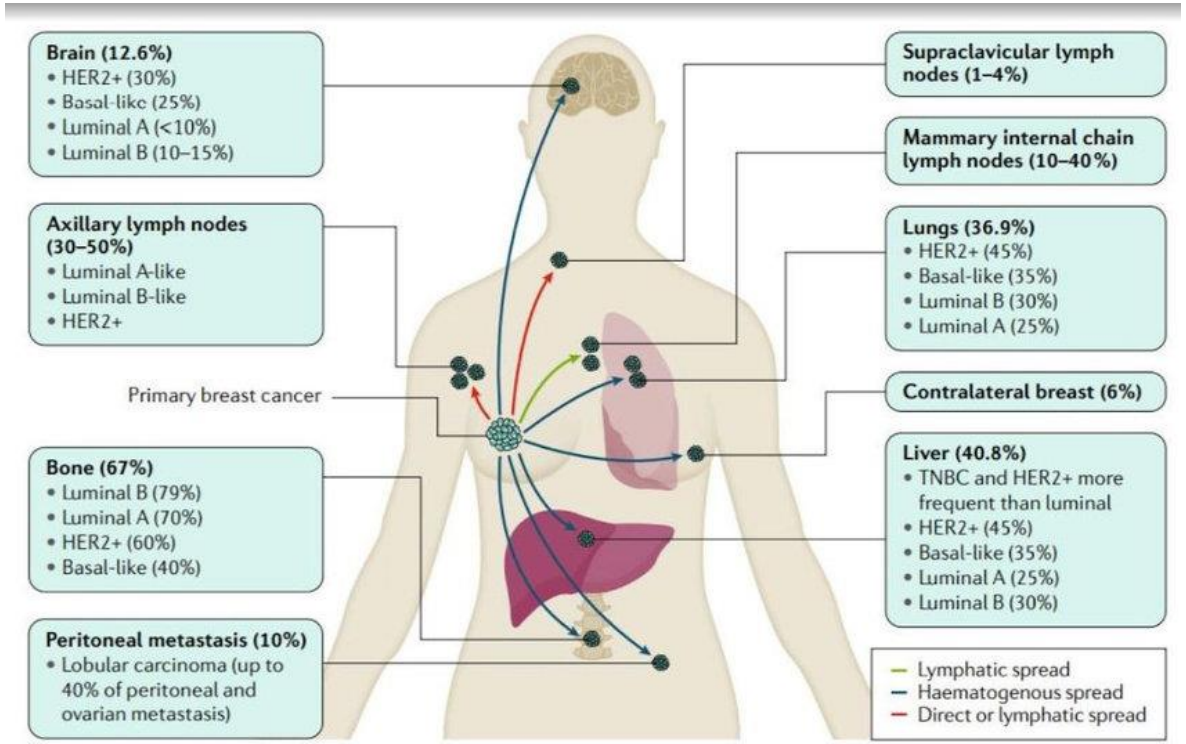
(E) Early dissemination
(C) Interactions/crosstalk
(D) Dormancy
(T) Responses to therapies

Opportunities to strengthen the MetNet:
Biology (primary/metastatic sites) and systems

- Mechanisms of early dissemination from pancreatic, prostate, lung, kidney, bladder or ovarian cancer
- Mechanisms associated with organotropism to the lung or bone
- Mechanisms associated with sequential metastases
- Contribution of neural signaling networks to metastasis in different secondary/tertiary sites
- Influence of the macroenvironment and host physiology, including co-morbid conditions, to metastasis

Opportunities to strengthen the MetNet:
Theme - Dormancy

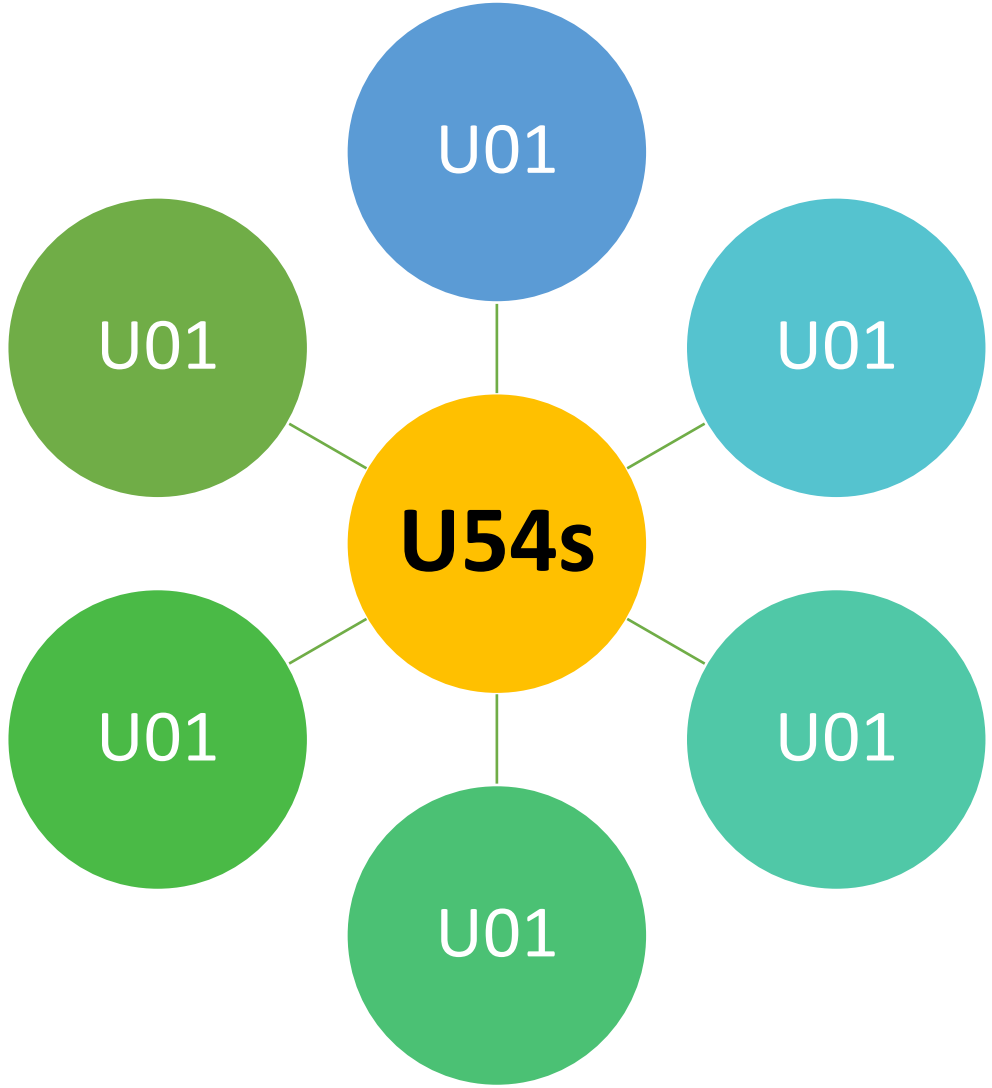
- Why dormancy?†
  - Effects both response and resistance to treatment, and patient outcomes
  - Multiple mechanisms involved in dormancy that would be best addressed by using systems level approaches
- Mechanisms associated with metastasis of breast cancer subtypes to multiple organs with different latencies
- Mechanisms associated with maintaining or releasing breast cancer or melanoma cells from dormancy
- How responses to standard-of-care, targeted or adjuvant therapies contribute to establishing, maintaining or emergence from a dormant state
- How the fate of dormant cells differs by organ, immune response, and other cell types



†BSA subcommittee question

Propose: Add U01 Research Projects to Strategically Build the MetNet

- Capitalize on the momentum and interest in using systems-level approaches to address questions in metastasis
- Encourage systems level approaches in areas, such as dormancy, that are poorly represented within the NCI portfolio



Portfolio analysis

- Dormancy†
  - Approximately 2-3% of the DCB Tumor Metastasis Branch portfolio (6/300)
  - QVR search revealed 11 awards of 192 competing applications in the NCI portfolio defined by keywords “metastasis AND dormancy” over the past 5 years.
- Systems approaches or systemic effects of cancer
  - Approximately 4-5% of the DCB Tumor Metastasis Branch portfolio (11/300)
  - QVR search revealed 6 awards of 129 competing applications in the NCI portfolio defined by keywords “metastasis AND systems biology” over the past 5 years.
- Other relevant programs:
  - CSBC, PS-ON, CCBIR
  - HTAN

†BSA subcommittee question

U01 Requirements:

- Apply systems level approaches to address one of the original MetNet FOA themes that will integrate and complement the MetNet Centers
    - Early dissemination
    - Interactions/crosstalk
    - Dormancy
    - Response to therapies
- Designate a Resource and Data Manager and an Administrative Manager
- Small set aside for pilot projects ($25K) in the out years

Benefit of Using Cooperative Agreement

- Align with U54 centers
  - Responsibilities and conduct
  - Participation requirements
  - Data sharing

- Programmatic involvement:
  - To facilitate intra-network collaboration
  - To ensure communication across interdisciplinary teams

Budget Considerations

- PAR, with no specific set-aside
  - Anticipated budget†
  - Cap requested budget at $500K/dc;
  - Award $415K direct costs/ approx., $700K/yr total costs (70% F&A)

- 2 receipt dates per year, 3 years

- Anticipate 2-3 applications selected for funding consideration each round using three criteria:
  - Programmatic priorities
  - Available funding
  - Meritorious impact score

†BSA subcommittee question

MetNet U01 Research Projects

Applying systems level approaches to address questions in metastasis to integrate and complement the MetNet